CLAIMS

1. An isolated polypeptide having fibulin-like activity selected from the group consisting of:

   a. the amino acid sequence recited in SEQ ID NO: 2;

   b. the mature form of the polypeptide whose sequence is recited in SEQ ID NO: 2 (SEQ ID NO: 4);

   c. active variants of the amino acid sequence given by SEQ ID NO: 2, wherein any amino acid specified in the chosen sequence is non-conservatively substituted, provided that no more than 15% of the amino acid residues in the sequence are so changed;

   d. the active fragment, precursor, salt, or derivative of the amino acid sequences given in a) to c).

2. The polypeptide of claim 1 that is a naturally occurring allelic variant of the sequence given by SEQ ID NO: 2 or SEQ ID NO: 4.

3. The polypeptide of claim 2, wherein the variant is the translation of a single nucleotide polymorphism.

4. The polypeptide of any one of claims 1 to 3, wherein the polypeptide binds specifically an antibody or a binding protein generated against SEQ ID NO: 2, SEQ ID NO: 4 or fragments thereof.

5. A fusion protein comprising a polypeptide according to any of the claims from 1 to 4.

6. The fusion proteins of claim 6 wherein said proteins further comprise one or more amino acid sequence belonging to these protein sequences: membrane-bound protein, immunoglobulin constant region, multimerization domains, extracellular proteins, signal peptide-containing proteins, export signal-containing proteins.

7. An antagonist of a polypeptide of any one of claims 1 to 4, wherein said antagonist comprises an amino acid sequence resulting from the non-conservative substitution and/or the deletion of one or more residues into the corresponding polypeptide.

8. A ligand which binds specifically to a polypeptide according to any one of claims 1 to 4.

9. The ligand of claim 8 that antagonizes or inhibits the fibulin-like activity of a polypeptide according to any one of claims 1 to 4.

10. A ligand according to claim 9 which is a monoclonal antibody, a polyclonal antibody, a humanized antibody, an antigen binding fragment, or the extracellular domain of a membrane-bound protein.

11. The polypeptide of any one of claims 1 to 6, wherein said polypeptides are in the form of active conjugates or complexes with a molecule chosen amongst radioactive labels, fluorescent labels, biotin, or cytotoxic agents.

12. A peptide mimetic designed on the sequence and/or the structure of a polypeptide according to any one of claims 1 to 4.

13. An isolated nucleic acid encoding for an isolated polypeptide selected from the group consisting of:

a) the polypeptides having fibulin-like activity of any one of claims 1 to 4;

b) the fusion proteins of claim 5 or 6; or

c) the antagonists of claim 7.

14. The nucleic acid of claim 13, comprising a DNA sequence consisting of SEQ ID NO: 1, or the complement of said DNA sequence.

15. A purified nucleic acid which:

a) hybridizes under high stringency conditions; or

b) exhibits at least about 85% identity over a stretch of at least about 30 nucleotides

with a nucleic acid selected from the group consisting of SEQ ID NO: 1, or a complement of said DNA sequence.

16. A vector comprising a nucleic acid as recited in any one of claims 13 to 15.

17. The vector of claim 16, wherein said nucleic acid molecule is operatively linked to expression control sequences allowing expression in prokaryotic or eukaryotic host cells of the encoded polypeptide.

18. A polypeptide encoded by the purified nucleic acid of any one of claims 13-15.

19. A process for producing cells capable of expressing a polypeptide of any one of claims from 1 to 7 or of claim 18, comprising genetically engineering cells with a vector or a nucleic acid according to any of the claims from 13 to 17.

20. A host cell transformed with a vector or a nucleic acid according to any of the claims from 13 to 17.

21. A transgenic animal cell that has been transformed with a vector or a nucleic acid according to any of the claims from 13 to 17, having enhanced or reduced expression levels of a polypeptide according to any one of claims 1 to 4.

22. A transgenic non-human animal that has been transformed to have enhanced or reduced expression levels of a polypeptide according to any one of claims 1 to 4.

23. A method for making a polypeptide of any one of claims from 1 to 7 comprising culturing a cell of claim 20 or 21 under conditions in which the nucleic acid or vector is expressed, and recovering the polypeptide encoded by said nucleic acid or vector from the culture.

24. A compound that enhances the expression level of a polypeptide according to any one of claims 1 to 4 into a cell or in an animal.

25. A compound that reduces the expression level of a polypeptide according to any one of claims 1 to 4 into a cell or in an animal.

26. The compound of claim 24 that is an antisense oligonucleotide or a small interfering RNA.

27. A purified preparation containing a polypeptide of any one of claims 1 to 6 or claim 18, an antagonist of claim 7, a ligand of any one of claims 8 to 10, peptide mimetic of claim 12, a nucleic acid of any one of claims 13 to 17, a cell of claim 20 or 21, or a compound of any one of claims 24 to 26.

28. Use of a polypeptide of any one of claims 1 to 6 or claim 18, a peptide mimetic of claim 12, a nucleic acid of any one of claims 13 to 17, a cell of claim 20 or 21, or a compound of claim 24, in the therapy or in the prevention of a disease when the increase in the fibulin-like activity of a polypeptide of any one of claims 1 to 4 is needed.

29. A pharmaceutical composition for the treatment or prevention of diseases needing an increase in the fibulin-like activity of a polypeptide of any one of claims 1 to 6 or claim 18, a peptide mimetic of claim 12, a nucleic acid of any one of claims 13 to 17, a cell of claim 20 or 21, or a compound of claim 24, as active ingredient.

30. Process for the preparation of a pharmaceutical composition, which comprises combining a polypeptide of any one of claims 1 to 6 or claim 18, a peptide mimetic of claim 12, a nucleic acid of any one of claims 13 to 17, a cell of claim 20 or 21, or a compound of claim 24, together with a pharmaceutically acceptable carrier.

31. Method for the treatment or prevention of a disease needing an increase in the fibulin-like activity of a polypeptide of any one of claims 1 to 4, comprising the administration of a therapeutically effective amount of a polypeptide of any one of claims 1 to 6 or claim 18, a peptide mimetic of claim 12, a nucleic acid of any one of claims 13 to 17, a cell of claim 20 or 21, or a compound of claim 24.

32. Use of an antagonist of claim 7, a ligand of any one of claims 8 to 10, or of a compound of claim 25 or claim 26, in the therapy or in the prevention of a

disease associated to the excessive fibulin-like activity of a polypeptide of any one of claims 1 to 4.

33. A pharmaceutical composition for the treatment or prevention of a disease associated to the excessive fibulin-like activity of a polypeptide of any one of claims 1 to 4, containing an antagonist of claim 7, a ligand of any one of claims 8 to 10, or of a compound of claim 25 or claim 26, as active ingredient.

34. Process for the preparation of pharmaceutical compositions for the treatment or prevention of diseases associated to the excessive fibulin-like activity of a polypeptide of any one of claims 1 to 4, which comprises combining an antagonist of claim 7, a ligand of any one of claims 8 to 10, or of a compound of claim 25 or claim 26, together with a pharmaceutically acceptable carrier.

35. A method for the treatment or prevention of diseases related to the polypeptide of any one of claims 1 to 4, comprising the administration of a therapeutically effective amount of an antagonist of claim 7, a ligand of any one of claims 8 to 10, or of a compound of claim 25 or claim 26.

36. A method for screening candidate compounds effective to treat a disease related to the fibulin-like polypeptides of any one of claims 1 to 4, comprising:

a) contacting a cell of claim 20, a transgenic animal cell of claim 21, or a transgenic non-human animal according to claim 22, having enhanced or reduced expression levels of the polypeptide, with a candidate compound and

b) determining the effect of the compound on the animal or on the cell.

37. A method for identifying a candidate compound as an antagonist/inhibitor or agonist/activator of a polypeptide of any one of the claims 1 to 4 comprising:

a) contacting said polypeptide, said compound, and a mammalian cell or a mammalian cell membrane capable of binding the polypeptide; and

b) measuring whether the molecule blocks or enhances the interaction of the polypeptide, or the response that results from such interaction, with the mammalian cell or the mammalian cell membrane.

38. A method for determining the activity and/or the presence of the polypeptide of any one of claims from 1 to 4 in a sample, the method comprising:

a) providing a protein-containing sample;

b) contacting said sample with a ligand of any one of claims 8 to 10; and

c) determining the presence or said ligand bound to said polypeptide.

39. A method for determining the presence or the amount of a transcript or of a nucleic acid encoding the polypeptide of any one of claims from 1 to 4 in a sample, the method comprising:

a) providing a nucleic acids-containing sample;

b) contacting said sample with a nucleic acid of any one of the claims 13 to 17; and

c) determining the hybridization of said nucleic acid with a nucleic acid into the sample.

40. Use of a primer derived from a nucleotide sequence as listed in SEQ ID NO:1 for determining the presence or the amount of a transcript or of a nucleic acid encoding a polypeptide of any one of claims from 1 to 4 in a sample by Polymerase Chain Reaction

41. A kit for measuring the activity and/or the presence of the fibulin-like polypeptides of any one of claims 1 to 4 in a sample comprising one or more of the following reagents: a polypeptide of any one of claims 1 to 6 or clam 18, an antagonist of claim 7, a ligand of any one of claims 8 to 10, a polypeptide of claim 11, a peptide mimetic of claim 12, a nucleic acid of any one of claims 13 to 17, a

cell of claim 20 or 21, a compound of any one of claims 24 to 26, a pharmaceutical composition of claims 29 or 33.